

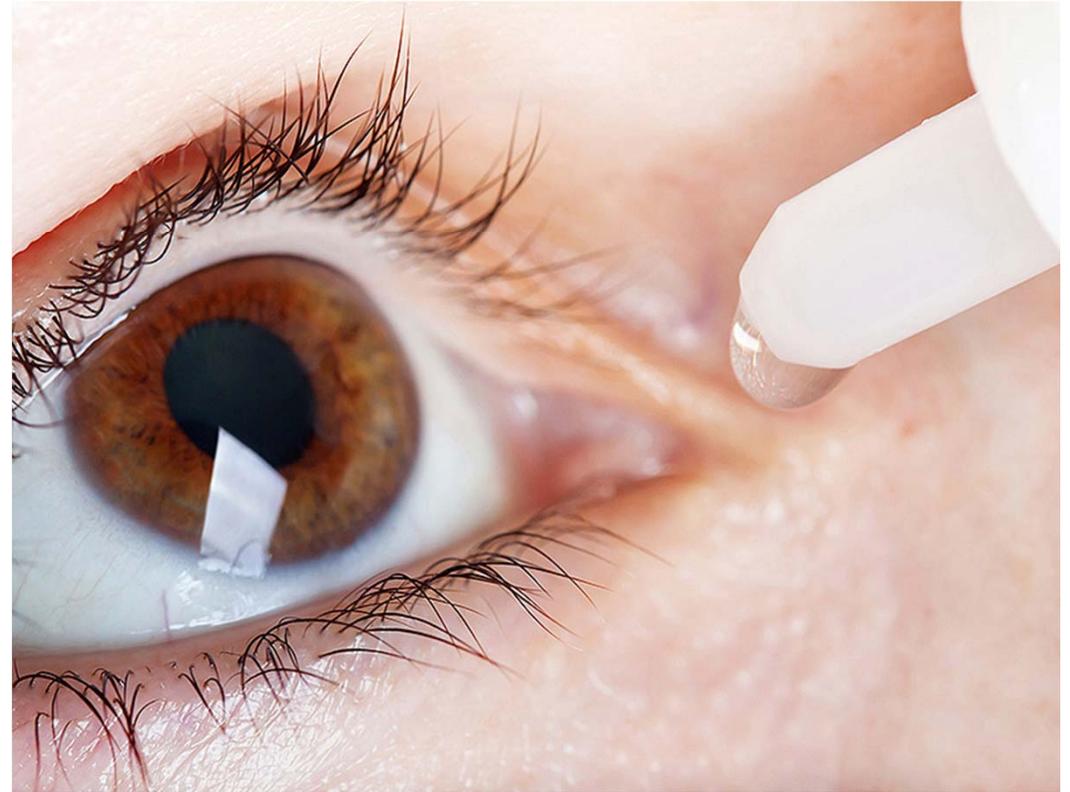
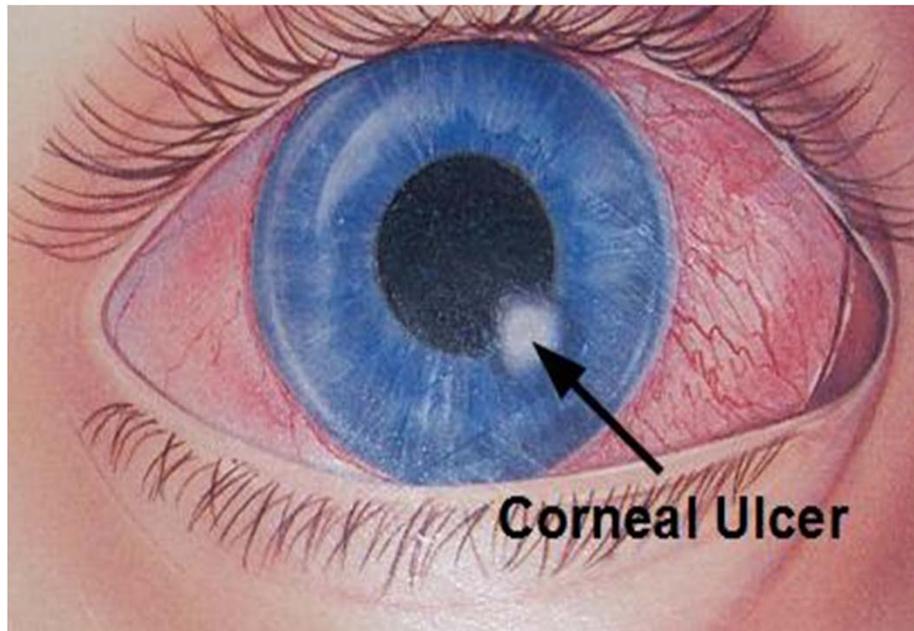
Plasminogen Deficiency Ligneous Conjunctivitis & Plasma Eye Drops

NICE Brisbane 2017
Rebecca Davidson



Serum eye drops

- Severe dry eye syndrome
- Non-healing corneal ulcers
- Recovery post LASIK surgery
- Usually autologous

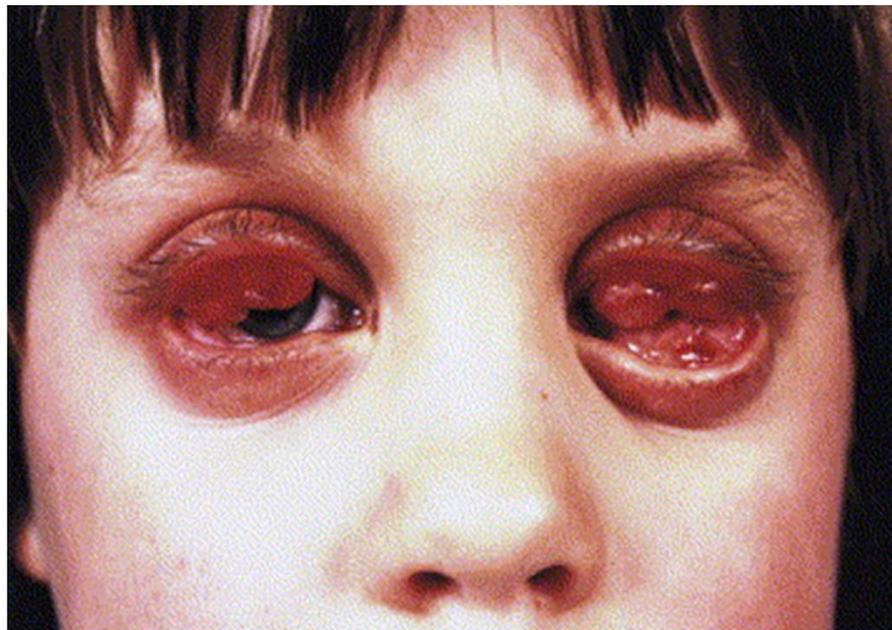


Frozen serum eye drops

Serum from a whole blood donation is fully segmented and then frozen as per a unit of FFP



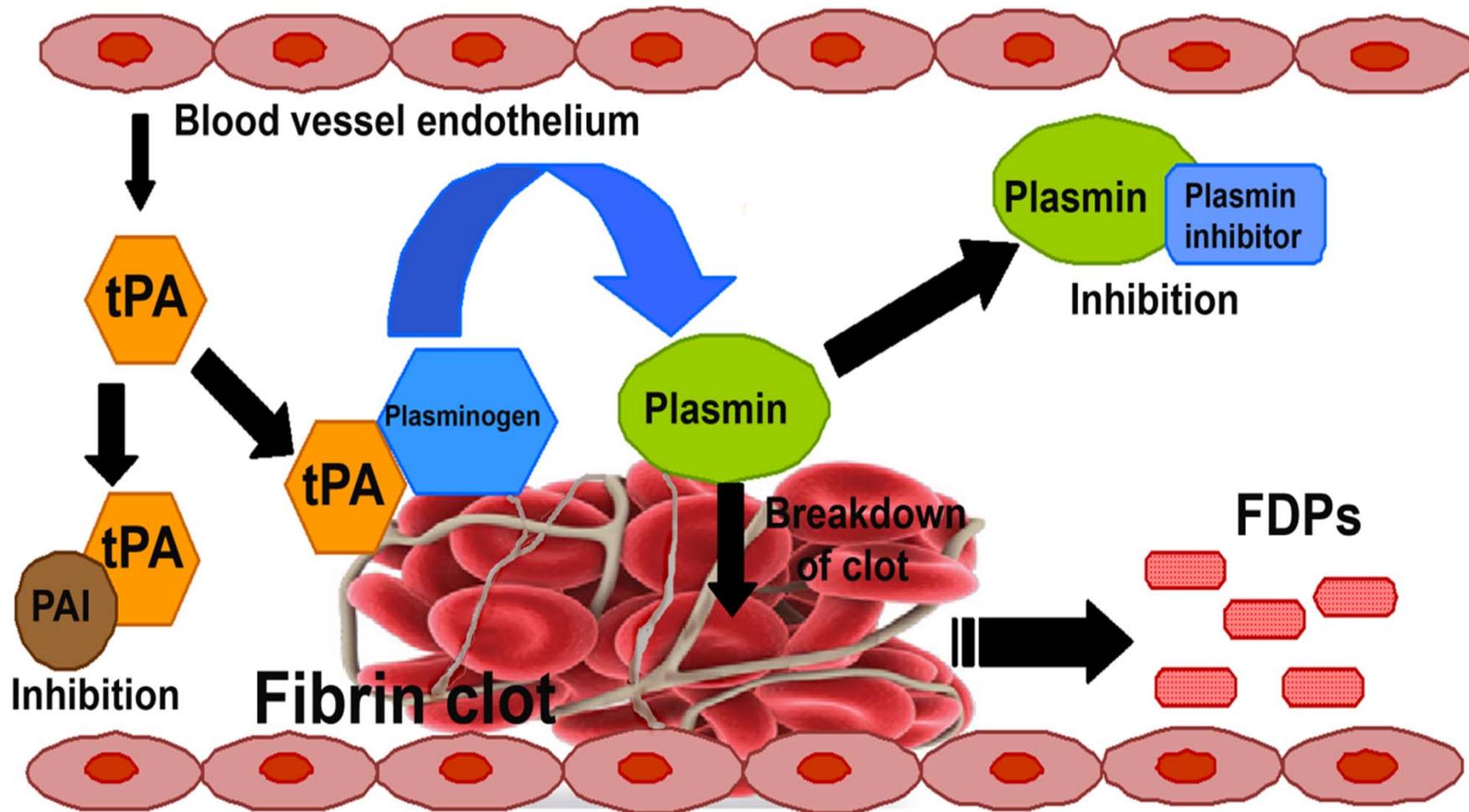
Ligneous Conjunctivitis



Plasminogen in tears

- Plasminogen activators in tear fluid convert plasminogen into plasmin, which rapidly clears the cornea of fibrin deposits
- In the absence of plasmin activity, fibrin-rich viscous or membranous material accumulates = ligneous conjunctivitis
- The wood like appearance is caused by the drying out of the fibrin and the products of the provoked inflammatory response

Fibrinolysis



Plasminogen Deficiency

- Congenital, rare
- 1-2 cases per million people
- Autosomal recessive inheritance of homozygous or compound heterozygous mutations in the plasminogen gene, *PLG*, located on chromosome 6q26
- first presentation of complications usually in the paediatric population

Common clinical manifestations

- Ligneous conjunctivitis – 80%
- Ligneous gingivitis – 80%
- Do not experience intravascular thromboembolic episodes despite severe deficiency of a key component of the fibrinolytic system

Less common clinical manifestations

- Tracheobronchial fibrin deposits impair the ciliary system of the tracheobronchial tree and support bacterial growth – 16%
- Fibrin deposition in the ears can occur – 14%
- Ligneous vaginitis – 8%
- Occlusive hydrocephalus caused by fibrin deposition in the cerebral ventricular system

Treatment of liginous conjunctivitis

Disappointing therapies:

- Hyaluronidase eye drops
- Corticosteroids
- Cyclosporine
- Immunosuppressants
- Antiviral agents
- Surgical resection – often causes accelerated recurrence of the pseudomembranes

Treatment of ligneous conjunctivitis

Variably effective therapies:

Topical solutions of-

Corticosteroids, heparin, fresh frozen plasma, plasminogen and immunosuppression.

Our patient – 4 year old Miss CC

- March 2016 – chronic membranous conjunctiva
- October 2016 - ?allergic/toxic, amyloid, ligneous, pyogenic granuloma
- 7 months after various treatments for chronic membranous conjunctival inflammation her grossly thickened conjunctival tissue was surgically resected

Histopathology of debrided membranes

- Pathologist's comment:

“Features of ligneous conjunctivitis with a pyogenic granuloma. The histological and clinical features are most suggestive of ligneous conjunctivitis associated with plasminogen deficiency and plasminogen gene mutations.”

- *“This condition usually manifests in children. There have been reports of successful treatment with fresh frozen plasma.”*

- This report lead the treating ophthalmologist to investigate the child's plasminogen activity
- ? therapeutic eye drops for topical replacement of plasminogen

Plasminogen activity

	Plasminogen level	Reference Range
Miss CC	0.14, 0.18	0.75-1.50 U/mL
Mother	0.72	0.75-1.50 U/mL
Father	0.52	0.75-1.50 U/mL

Plasma eye drops

- Plasma from her parents was considered unsuitable as both were found to have slightly low plasminogen levels
- A screened donor was considered the better option
- With input from Monash Health Paediatric Haematologists, the ARCBS TMS and the ARCBS product preparation team an appropriate donation of apheresis, group matched, CMV negative plasma was collected.

Frozen plasma eye drops



References

[Marks DC](#)¹, [Fisher J](#)², [Mondy P](#)², [Segatchian J](#)³, [Dennington PM](#)². Serum eye drop preparation in Australia: Current manufacturing practice. *Transfus Apher Sci* 2015;53(1):92-4

Magdum R, Gahlot A, Mushtaq I, Iqbal B, Arun S. Ligneous conjunctivitis: A rare case report. *Trop J Med Res* 2015;18:119-120

Heidemann DG, Williams GA, Hartzler M, Ohanian A, Citron ME. Treatment of ligneous conjunctivitis with topical plasmin and topical plasminogen. *Cornea*. 2003;22:760–762.

Watts P, Suresh P, Mezer E, et al. Effective treatment of ligneous conjunctivitis with topical plasminogen. *Am J Ophthalmol*. 2002;133:451–455.

Pergantou H, Likaki D, Fotopoulou M, Katsarou O, Xafaki P, Platokouki H. Management of ligneous conjunctivitis in a child with plasminogen deficiency. *Eur J Pediatr*. 2011;170:1333-1336.

Tabarra KF. Prevention of ligneous conjunctivitis by topical and subconjunctival fresh frozen plasma. *Am J Ophthalmol*. 2004;138(2):299-300.

Shuster V, Hügle B, Tefs K. Plasminogen deficiency. *J Thromb Haemost*. 2007;5(12):2315-2322.